standard techniques. The active agent must be stable to passage through the gastrointestinal tract. If necessary, suitable agents for stable passage can be used, and may include phospholipids or lecithin derivatives described in the literature, as well as liposomes, microparticles (including microspheres and macrospheres).

For parenteral administration, the compound may dissolved in a pharmaceutical carrier and administered as either a solution or a suspension. Illustrative of suitable carriers are water, saline, dextrose solutions, fructose solutions, ethanol, or oils of animal, vegetative or synthetic origin. The carrier may also contain other ingredients, for example, preservatives, suspending agents, solubilizing agents, buffers and the like. When the compounds are being administered intracerebroventricularly or intrathecally, they may also be dissolved in cerebrospinal fluid.

In the treatment of cancer (sarcomas, carcinomas or leukemias), a distinction can be made between the types of systemic adjuvant chemotherapies that are typically used in concert with the more extreme methods of surgical excision and radiation therapy. There are two broad classes of chemotherapeutic adjuvants: (1) endocrine and antivasogenic therapeutic agents which are aimed at altering the body's physiology; and (2) cytotoxic chemotherapeutic agents which are typically administered systemically to kill or inhibit the growth of transformed cells.

Cytotoxic or antineoplastic agents are represented by a number of drug classes. Alkylating agents undergo chemical reactions that generate highly reactive electrophilic carborationsnium ions that readily form covalent linkages (alkylate) with various nucleophilic biologically important moieties such as nucleic acid bases and phosphate, amine, sulfhydryl, hydroxyl, carboxyl and imidazole groups. These agents, among other functions, have cytotoxic actions that disturb the fundamental mechanisms concerned with cell growth, mitotic activity, differentiation and function. Chlorambucil, modified busulfan, cyclophosphamide, ifosfamide and cisplatin and its structural analogs are representative alkylating agents.

Antimetabolites such as folic acid analogs (e.g. methotrexate) and pyrimidine analogs (e.g. fluorouracil and fluorodeoxyuridine) exert cytotoxic activity by blocking or preventing metabolic pathways leading to neoplastic cell destruction. Methotrexate is also known to be useful in the treatment of psoriasis by inhibiting the proliferation of epidermal cells.

Another potent cytotoxic class is mitotic inhibitors such as the paclidaxel or the alkaloids camptothecin, vincristine and vinblastine.

Also, certain antibiotics, such as doxorubicin and daunorubicin, (tetracyclic aglycone glycosides), intercalcate with DNA and inhibit nucleic acid synthesis.

In accordance with the present invention, bioconjugates for the treatment of cancer are formed preferably using chemotherapeutics selected from the group consisting of alkylating agents, antimetabolites and mitotic inhibitors. For example, methotrexate is an antimetabolite; chlorambucil, cisplatin and modified busulfan are alkylating agents, and camptothecin and its derivatives are alkaloids. The bioconjugates formed from these cytotoxic agents can be administered intravenously for the treatment of the specific classes of cancer for which they are known to be effective, e.g. cancer of the colon, lung, kidney, breast, prostate, melanoma, nasopharyngeal, T-cell leukemia, myelogenous leukemia, lymphocytic leukemia and the like. When delivered intravenously to the blood stream and the bioconjugates contain cobalamin, the natural affinity of cancer cells for B_{12} will target the bioconjugates to these tissues or cell sites. Alternatively, the bioconjugates can be engineered to be selective for the delivery of the chemotherapeutic agent to the desired cancer cell by the incorporation of a suitable targeting molecule (such as those set forth above) on the organocobalt complex.

In accordance with the present invention, solid tumors are treated as follows, with use of a drug-B_{12} bioconjugate as an example. This example is not intended to limit the present invention in any manner, and a skilled artisan could readily determine other bioconjugates of the present invention which could be utilized for the treatment of solid tumors. The drug-B_{12} bioconjugate is administered, preferably intravenously, to a cancer patient to target metastatic cancer when the cancer cell has a significant requirement for cobalamin. This propensity of cobalamins to migrate to the cancer cells significantly reduces cardiotoxicity, myelotoxicity, hepatotoxicity and similar side effects that limit the size and frequency of effective dosing of antineoplastic agents. Furthermore, problems associated with toxicity to non-targeted cells is minimized. Delivery is further enhanced by the triggering of the release of the antineoplastic agent from the bioconjugate by the mechanism of photolysis or sonolysis which provides for a high degree of spatial and temporal control of the drug release at a localized area over a short time. The application of a magnetic field with photolysis further serves to protect health cells by recombination of the bioconjugate and limit the release of active agent to the specific cancer cell-containing site(s).

Although chemotherapy is generally reserved for targeting metastasized cells after the surgical excision of the primary tumor mass, the triggered release of a bioactive agent drawn to the tumor site allows for treatment of the primary tumor, as well as metastatic neoplasms that have spread to a limited and known area. The bioconjugate dosage, length of treatment, degree of photoactivation, and other treatment parameters can be determined by one skilled in the art based on the type of cancer, antineoplastic agent administered, specific cobalamin used, condition of the patient and other factors which are variable and best determined on a case-by-case basis.

In accordance with the present invention, leukemia is treated as follows, with use of a drug-B_{12} bioconjugate as an example. This example is not intended to limit the present invention in any manner, and a skilled artisan could readily determine other bioconjugates of the present invention which could be utilized for the treatment of leukemia. At least two forms of leukemia, chronic myeloid leukemia (CML) and acute promyeloctyic leukemia (APL), produce high levels of B_{12} binding proteins that result in a 3- to 36-fold increase in the unsaturated B_{12} binding capacity in the blood. The increased concentration of B_{12} binding proteins is consistent with the rapid turnover of immature blood cells and provides an opportunity to target the delivery of antileukemic drugs, such as bis-alkylating agents derived from busulfan, to the transformed hematopoietic cells responsible for the leukemic condition. The bioconjugates of this invention provide a means for the effective administration of such alkylating agents to cell sites from which the active agent can be released from the conjugate. This targeted delivery and release provides a significant advance in the treatment of CML and APL, for which current chemotherapy methods sometimes provide incomplete remission.

The present invention is also useful for the treatment of psoriasis. Psoriasis is a prime target for the transdermally or orally controlled delivery of antimetabolites activated by photolytically induced cleavage. Although not life-threatening, psoriasis can significantly diminish the quality of life of patients who experience severe exfoliation associated with psoriatic and rheumatoid arthritis. Antimetabolites, such as methotrexate and 5-fluorouracil, are effective in controlling severe cases of skin proliferation. Effective oral therapy is limited by hepatotoxicity in spite of low dosing, and the risk of cumulative liver damage requires such therapy to be reserved for only the most severe episodes during a patient's life. The delivery of